Contains Nonbinding Recommendations

Draft Guidance on Nebivolol Hydrochloride

This draft guidance, once finalized, will represent the Food and Drug Administration's (FDA's) current thinking on this topic. It does not create or confer any rights for or on any person and does not operate to bind FDA or the public. You can use an alternative approach if the approach satisfies the requirements of the applicable statutes and regulations. If you want to discuss an alternative approach, contact the Office of Generic Drugs.

Active ingredient: Nebivolol Hydrochloride

Form/Route: Tablets/Oral

Recommended studies: 2 studies

1. Type of study: Fasting
   Design: Single-dose, two-way crossover *in vivo*
   Strength: 20 mg
   Subjects: Normal healthy males and females, general population.
   Additional Comments: Females should not be pregnant or lactating, and if applicable, should practice abstention or contraception during the study.

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2. Type of study: Fed
   Design: Single-dose, two-way crossover *in vivo*
   Strength: 20 mg
   Subjects: Normal healthy males and females, general population.
   Additional Comments: Females should not be pregnant or lactating, and if applicable, should practice abstention or contraception during the study.

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*Note: As an option, due to the relatively long half-life of nebivolol, these studies may be conducted using a parallel design. As an additional option for either the crossover or parallel design, is to truncate the AUC at 72 hours.

Analytes to measure (in appropriate biological fluid): Racemic nebivolol

Bioequivalence based on (90% CI): Racemic nebivolol

Waiver request of *in vivo* testing: 2.5 mg, 5 mg, and 10 mg based on (i) acceptable bioequivalence studies on the 20 mg strength, (ii) proportional similarity of the 2.5 mg, 5 mg, 10 mg, and 20 mg strengths, and (iii) acceptable *in vitro* dissolution testing of the 2.5 mg, 5 mg, 10 mg, and 20 mg strengths.

Dissolution test method and sampling times:

Please note that a **Dissolution Methods Database** is available to the public at the OGD website at http://www.accessdata.fda.gov/scripts/cder/dissolution/. Please find the dissolution information for this product at this website. Please conduct comparative dissolution testing on 12 dosage units each of all strengths of the test and reference products. Specifications will be determined upon review of the application.